

- ✓ 1. A matrix for implantation in a mammalian host comprising:

biodegradable, biocompatible, mineral-free Type-I insoluble bone collagen particles, xenogenic to said host, said particles being depleted in noncollagenous protein, having a mean diameter within the range of 70 μ m to 850 μ m, and an intraparticle surface area greater than the surface area of native demineralized bone powder.

- ✓ 2. A matrix for implantation in a mammalian host comprising deglycosylated Type-I mineral-free, insoluble bone collagen, xenogenic to said host, and biodegradable and biocompatible therewithin.

- ✓ 3. A matrix for implantation in a mammalian host comprising:

particles consisting essentially of biodegradable, biocompatible mineral-free Type-I bone collagen, xenogenic to said host, depleted in noncollagenous protein, and treated with a swelling agent to increase the intraparticle surface area and intraparticle porosity thereof.

4. The matrix of claim 1, 2, or 3 comprising packed particles.

5. The matrix of claim 4 wherein said particles have a mean diameter within the range of 70 μ m to 850 μ m, define intraparticle pores, and an intraparticle surface area greater than the surface area of native demineralized bone powder.

6. The matrix of claim 4 wherein said particles have a mean diameter within the range of 150 μ m to 420 μ m.

7. The matrix of claim 1 or 3 wherein said particles are deglycosylated.

8. The matrix of claim 4 wherein the particles define interstices dimensioned to permit influx, proliferation and differentiation of migratory cells from the body of said mammalian host.

9. The matrix of claim 8 further comprising dispersed osteogenic protein, said matrix being capable of inducing endochondral bone formation when implanted in said mammalian host.

10. The matrix of claim 9 wherein said matrix is shaped to span a non-union fracture in said mammalian host.

11. The matrix of claim 1, 2, or 3 further comprising a therapeutic drug adsorbed onto the surface thereof for sustained release in said mammalian host.

12. The matrix of claim 4 wherein said particles are incubated with a swelling agent followed by washing to remove soluble components.

13. The matrix of claim 12 wherein said swelling agent is an organic protein denaturant.

14. The matrix of claim 12 wherein said swelling agent is dichloromethane.

15. The matrix of claim 12 wherein said swelling agent is hydrogen fluoride.

16. The matrix of claim 12 wherein said swelling agent is trifluoroacetic acid.

17. The matrix of claim 12 wherein said swelling agent is dichloromethane, acetonitrile, or isopropanol mixed with 0.1%-10% trifluoroacetic acid.

18. The matrix of claim 12 wherein said swelling agent is isopropanol.

19. The matrix of claim 12 wherein said swelling agent is acetonitrile.

Sub B1
20. A method of manufacturing a biocompatible, in vivo biodegradable matrix suitable for implantation in a mammalian host, said method comprising the steps of:

Sub B, cont

A. providing demineralized bone particles xenogenic to said host, having a mean particle diameter within the range of 70 μ m to 850 μ m;

B. contacting the particles with a swelling agent to increase the intraparticle surface area and intraparticle porosity; and

C. washing said particles to reduce the non-collagenous protein components thereof.

21. The method of claim 20 comprising the additional step of extracting protein from said particles with guanidine prior to step B.

2 22. The method of claim 20 wherein the swelling agent used in step B is hydrogen fluoride.

3 23. The method of claim 20 wherein the swelling agent used in step B is trifluoroacetic acid.

4 24. The method of claim 20 wherein the swelling agent used in step B is acetonitrile.

5 25. The method of claim 20 wherein the swelling agent used in step B is isopropanol.

6 26. The method of claim 20 wherein the swelling agent used in step B is acetonitrile, isopropanol, 14 dichloromethane mixed with 0.1%-10% trifluoroacetic acid.

1
727. The method of claim 20 wherein the swelling agent used in step B is dichloromethane.

828. The method of claim 20 wherein the particles are washed with a saline buffer in step C.

929. The method of claim 20 wherein the particles are washed with a urea-containing buffer and water in step C.

Sub B2
30. The method of claim 20 comprising the additional step of adsorbing osteogenic protein onto said particles.

1131. The method of claim 30 wherein the osteogenic protein is adsorbed onto said particles by precipitation in cold ethanol.

1232. The method of claim 30 wherein the osteogenic protein is adsorbed onto said particles by incubation in a solution comprising acetonitrile and trifluoroacetic acid, followed by lyophilization.

1333. The method of claim 30 wherein the osteogenic protein present in culture medium is adsorbed onto said particles by incubation, followed by lyophilization.

82
1434. The method of claim 20 wherein the particles have a mean diameter within the range of 150 μ m to 420 μ m.

38